

Applicants: Meir Shinitzky, et al.
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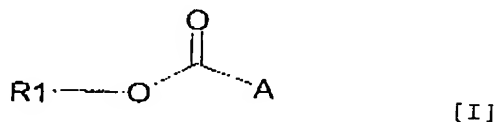
Amendments to the Claims:

Please cancel claims 1-48 and 73-134 without disclaimer or prejudice to applicants' right to pursue the subject matters of these claims in the future.

Pursuant to 37 C.F.R. §1.121(c), this listing of claims will replace all prior versions, and listings, of claims in the application:

1-48. (Cancelled)

49. (Original) A method for the treatment of inflammation which comprises administering to an individual in need thereof, an effective amount of a compound of the general formula I:



or of a pharmaceutically acceptable salt thereof, wherein R1 is C₁₂-C₂₄ alkyl or C₁₀-C₂₄ alkenyl, and A is a residue containing at least one acyclic or cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom.

50. (Original) The method according to claim 49 wherein R1 is a C₁₂-C₂₀ alkyl or alkenyl.

51. (Original) The method according to claim 50 wherein R1 is a C₁₆-C₁₈ alkyl or alkenyl.

52. (Original) The method according to claim 51 wherein R1 is

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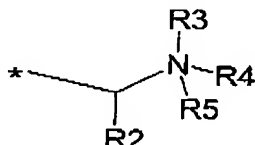
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hexadecyl, octadecyl, hexadecenyl, octadecenyl, cis-9-octadecenyl, trans-9-octadecenyl, cis-9,12-octadecadienyl, cis-6,9,12-octadecatrienyl, or cis-9,12,15-octadecatrienyl,

53. (Original) The method according to claim 52 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.
54. (Currently Amended) The method according to ~~any one of~~ claims 49 ~~to 53~~ wherein in said compound of formula I the residue A is selected from the group consisting of:
- (i)



wherein R2 is H, C₁-C₆ alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR₆R₇, or CR₈R₈NR₆R₇; R3 is H, a pair of electrons or C₁-C₆ alkyl; R4 and R5 each independently is H or C₁-C₆ alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl; and R6, R7 and R8 each independently is H or C₁-C₆ alkyl;

(ii) phenyl substituted by NR₆R₇ or CR₈R₈NR₆R₇, wherein R6, R7 and R8 each is independently H or C₁-C₆ alkyl; and

(iii)

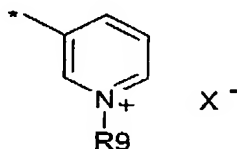
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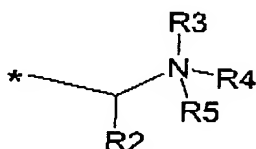
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wherein R9 is H, C₁-C₆ alkyl or indolyl(C₁-C₄)alkyl, and X⁻ is a counter ion, or R9 is a pair of electrons and X is absent.

55. (Original) The method according to claim 54 wherein the residue A is of the formula:



wherein R2 is H; a straight or branched C₁-C₆ alkyl selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, pentyl and hexyl; phenyl, benzyl or p-hydroxybenzyl; R3 is H, a pair of electrons or C₁-C₆ alkyl; R4 and R5 is each independently H or C₁-C₆ alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl, said ring being selected from the group consisting of pyrrolidine, piperidine, morpholine, piperazine, and 4-methylpiperazine.

56. (Original) The method according to claim 55 wherein R2 is H or phenyl, R3 is H or a pair of electrons, R4 and R5 are each H or C₁-C₆ alkyl, or R4 and R5 together with the

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N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 1 or 4 by methyl.

57. (Original) The method according to claim 56 wherein said compound is selected from the group consisting of:

N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;

(4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;

(4-Methyl-piperazin-1-yl)-acetic acid octadecyl ester tartrate;

4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;

α -Amino- α -phenyl-acetic acid octadec-(Z)-9-enyl ester HCl salt; and

Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.

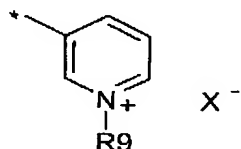
58. (Original) The method according to claim 54 wherein the residue A is phenyl substituted by NR6R7 or CR8R8NR6R7, wherein R6, R7 and R8 is each independently H or C₁-C₆ alkyl.

59. (Original) The method according to claim 58 wherein A is phenyl substituted by CR8R8NR6R7, wherein R8 is H and R6 and R7 is each methyl.

60. (Original) The method according to claim 59, wherein said compound is 4-dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl or 4-dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.

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61. (Original) The method according to claim 54 wherein A is the group:



wherein R9 is H, C₁-C₆ alkyl or indolyl(C₁-C₄)alkyl and X⁻ is a counter ion, or R9 is a pair of electrons and X⁻ is absent.

62. (Original) The method according to claim 61 wherein R9 is a pair of electrons and X⁻ is absent, or R9 is methyl or indolyethyl and X⁻ is a counter ion selected from the group consisting of chloride, bromide, iodide and tosylate.
63. (Original) The method according to claim 62 wherein said compound is selected from the group consisting of:
- Nicotinic acid octadec-(Z)-9-enyl ester;
 - 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;
 - 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium chloride;
 - 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium tosylate; and
 - 1-[(2-(1H-indol-3-yl)-ethyl)-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium bromide.

64. (Currently Amended) The method according to ~~any one of~~ claims 49 ~~to 63~~ for treatment of immunologically-mediated inflammation.

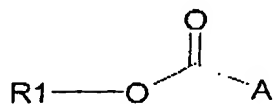
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65. (Original) The method according to claim 64 for the treatment of an immunologically-mediated chronic or acute inflammatory disease, disorder or condition.
66. (Original) The method according to claim 65 for the treatment of an autoimmune disease, a severe allergy, asthma, or an inflammation associated with a disease, disorder or condition selected from graft rejection, a chronic degenerative disease such as Alzheimer's disease, neuroprotection, organ regeneration, chronic ulcers of the skin, or schizophrenia.
67. (Original) The method according to claim 66 wherein said autoimmune disease, disorder or condition is multiple sclerosis or a human arthritic condition.
68. (Original) The method according to claim 67 wherein said human arthritic condition is rheumatoid arthritis, reactive arthritis with Reiter's syndrome, ankylosing spondylitis or other inflammation of the joints mediated by the immune system.
69. (Original) The method according to claim 65 wherein said immunologically-mediated inflammatory disease, disorder or condition is myasthenia gravis, Guillain-Barré syndrome, or other inflammatory disease of the nervous system; psoriasis, pemphigus vulgaris or other diseases of the skin; systemic lupus erythematosus, glomerulonephritis or other disease affecting the kidneys; atherosclerosis or other inflammation of the blood vessels; autoimmune hepatitis, inflammatory bowel diseases, pancreatitis, or other disorder of the gastrointestinal system; type 1 diabetes mellitus,

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autoimmune thyroiditis, or other disease of the endocrine system.

70. (Original) The method according to claim 69 wherein said immunologically-mediated inflammatory disease or disorder is psoriasis.
71. (Currently Amended) The method according to ~~any one of~~ claims 49 ~~to 70~~ wherein said compound is administered by oral, topical, intradermal or parenteral route.
72. (Original) The method according to claim 71 wherein said compound is administered by subcutaneous, intravenous, or intramuscular route.
- 73-134. (Cancelled)
135. (Original) A method of treating a T-cell mediated disease, disorder or condition, which comprises administering to an individual in need an effective amount of a therapeutic preparation comprising an antigen recognized by inflammatory T cells associated with the pathogenesis of said T-cell mediated disease, disorder or condition, and an adjuvant of the general formula Ia:



[Ia]

or a pharmaceutically acceptable salt thereof, wherein R1 is C₁₀-C₂₄ alkyl or C₁₀-C₂₄ alkenyl, and A is a residue containing at least one acyclic or cyclic amino group and/or at least one heteroaromatic ring containing

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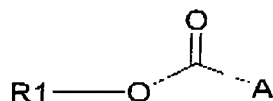
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a tertiary or quaternary nitrogen atom, but excluding the compounds wherein R1 is C₁₈ alkyl and A is a residue containing at least one acyclic amino group or -CO-A is the residue of proline.

136. (Original) A method of causing a shifting of T-cell cytokine response from T_H1 to T_H2 in an individual suffering from a T-cell mediated disease, disorder or condition, which comprises administering to said individual in need an effective amount of a therapeutic preparation comprising an antigen recognized by inflammatory T cells associated with the pathogenesis of said T-cell mediated disease, disorder or condition and an adjuvant of the general formula Ia:



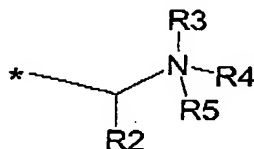
[Ia]

or a pharmaceutically acceptable salt thereof, wherein R1 is C₁₀-C₂₄ alkyl or C₁₀-C₂₄ alkenyl, and A is a residue containing at least one acyclic or cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, but excluding the compounds wherein R1 is C₁₈ alkyl and A is a residue containing at least one acyclic amino group or -CO-A is the residue of proline.

137. (Original) The method according to claim 136 wherein said therapeutic preparation causes a decrease in IL-2 or IFN- γ T-cell cytokine response and an increase in IL-4 or IL-10 T-cell cytokine response.

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138. (Currently Amended) The method according to claim 135 ~~or~~
136 wherein R1 is a C₁₂-C₂₀ alkyl or alkenyl.
139. (Original) The method according to claim 138 wherein R1
is a C₁₆-C₁₈ alkyl or alkenyl.
140. (Original) The method according to claim 139 wherein R1
is hexadecyl, octadecyl, hexadecenyl, octadecenyl, cis-9-
octadecenyl, trans-9-octadecenyl, cis-9,12-
octadecadienyl, cis-6,9,12-octadecatrienyl, or cis-
9,12,15-octadecatrienyl,
141. (Original) The method according to claim 140 wherein R1
is cis-9-octadecenyl or trans-9-octadecenyl.
142. (Currently Amended) The method according to ~~any one of~~
~~claims 135 to 141~~ wherein in said compound of formula Ia
the residue A is selected from the group consisting of:
- (i)



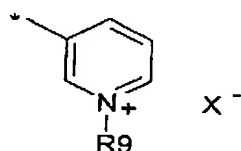
wherein R2 is H, C₁-C₆ alkyl, aryl or aralkyl,
wherein any aryl moiety may be unsubstituted or
substituted by nitro, cyano, halo, hydroxy, NR₆R₇, or
OR₈SR₈NR₆R₇; R3 is H, a pair of electrons or C₁-C₆ alkyl;
R4 and R5 is each independently H or C₁-C₆ alkyl, or R4
and R5 together with the nitrogen atom to which they are
attached form a 5-7 membered saturated ring optionally
interrupted by an oxygen atom or by a nitrogen atom

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optionally substituted by C₁-C₆ alkyl, provided that R₄ and R₅ are not H or C₁-C₆ alkyl when R₁ is octadecyl; and R₆, R₇ and R₈ is each independently H or C₁-C₆ alkyl;

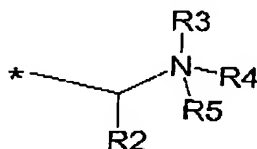
(ii) phenyl substituted by NR₆R₇ or CR₈R₈NR₆R₇, wherein R₆, R₇ and R₈ each is independently H or C₁-C₆ alkyl; and

(iii)



wherein R₉ is H, C₁-C₆ alkyl or indolyl(C₁-C₄)alkyl, and X⁻ is a counter ion, or R₉ is a pair of electrons and X is absent.

113. (Original) The method according to claim 142 wherein the residue A has the formula:



wherein R₂ is H; a straight or branched C₁-C₆ alkyl selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, pentyl and hexyl; phenyl, benzyl or p-hydroxybenzyl; R₃ is H, a pair of electrons or C₁-C₆ alkyl; R₄ and R₅ is each independently H or C₁-C₆ alkyl, or R₄ and R₅ together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an

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oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl, said ring being selected from the group consisting of pyrrolidine, piperidine, morpholine, piperazine, and 4-methylpiperazine, provided that R₄ and R₅ are not H or C₁-C₆ alkyl when R₁ is octadecyl.

144. (Original) The method according to claim 143 wherein R₂ is H or phenyl, R₃ is H or a pair of electrons, R₄ and R₅ is each H or C₁-C₆ alkyl, or R₄ and R₅ together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 1 or 4 by methyl, provided that R₄ and R₅ are not H or C₁-C₆ alkyl when R₁ is octadecyl.

145. (Original) The method according to claim 144 wherein said adjuvant is selected from the group consisting of:

N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;

(4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;

4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;

α -Amino- α -phenyl-acetic acid octadec-(Z)-9-enyl ester HCl salt; and

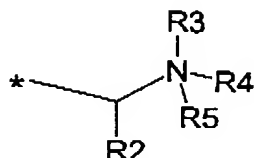
Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.

146. (Currently Amended) The method according to claim 135 ~~or~~ ~~136~~ wherein R₁ is C₁₈ alkyl and A is a residue containing at least one cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, but excluding the compound wherein -CO-A is the residue of proline.

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147. (Original) The method according to claim 146 wherein the residue A has the formula:

(i)



wherein R2 is H, C₁-C₆ alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR₆R₇, or CR₈R₈NR₆R₇; R3 is H, a pair of electrons or C₁-C₆ alkyl; R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl; and R6, R7 and R8 is each independently H or C₁-C₆ alkyl.

148. (Original) The method according to claim 147 wherein R2 is H or phenyl, R3 is H or a pair of electrons, and R4 and R5 together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 1 by methyl.

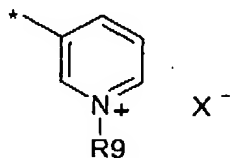
149. (Original) The method according to claim 143 wherein said adjuvant is (4-methyl-piperazin-1-yl)-acetic acid octadecyl ester tartrate.

150. (Original) The method according to claim 142 wherein A is phenyl substituted by NR₆R₇ or CR₈R₈NR₆R₇, wherein R6, R7

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and R8 is each independently H or 1 C₁-C₆ alkyl.

151. (Original) The method according to claim 150 wherein A is phenyl substituted by CR₈R₈NR₆R₇, wherein R8 is H and R6 and R7 is each methyl.
152. (Original) The method according to claim 151 wherein said adjuvant is 4-dimethylaminomethyl-benzoic acid octadec-(Z)-9-enyl ester HCl or 4-dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.
153. (Original) The method according to claim 142 wherein A is the group:



wherein R9 is H, C₁-C₆ alkyl or indolyl(C₁-C₄)alkyl and X⁻ is a counter ion, or R9 is a pair of electrons and X⁻ is absent.

154. (Original) The method according to claim 153 wherein R9 is a pair of electrons and X⁻ is absent, or R9 is methyl or indolylethyl and X⁻ is a counter ion selected from the group consisting of chloride, bromide, iodide and tosylate.
155. (Original) The method according to claim 154 wherein said adjuvant is selected from the group consisting of:
- Nicotinic acid octadec-(Z)-9-enyl ester;
 - 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;

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1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium
chloride;

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium
tosylate; and

1-[(2-(1H-indol-3-yl)-ethyl)-3-octadec-(Z)-9-
enyloxycarbonyl-pyridinium bromide.

156. (Currently Amended) The method according to ~~any one of~~
claims 135 ~~to 155~~ wherein said antigen raises a humoral
response in said individual.
157. (Currently Amended) The method according to ~~any one of~~
claims 135 ~~to 155~~ wherein said antigen raises a cellular
response in said individual.
158. (Currently Amended) The method according to ~~any one of~~
claims 135 ~~to 155~~ wherein said T-cell mediated disease is
an autoimmune disease and said antigen is a peptide.
159. (Original) The method according to claim 158, wherein said
autoimmune disease is an organ-specific autoimmune
disease.
160. (Original) The method according to claim 159 wherein said
organ-specific autoimmune disease is type I diabetes
mellitus, multiple sclerosis, rheumatoid arthritis or
autoimmune thyroiditis.
161. (Original) The method according to claim 160 for the
treatment of multiple sclerosis wherein said antigen is a
peptide derived from the sequence of myelin basic protein
(MBP) or an analogue thereof that is recognized by T-
cells involved in the pathogenesis of multiple sclerosis.

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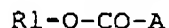
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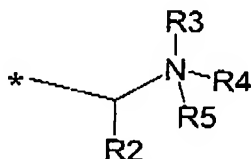
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162. (Original) The method according to claim 160 for the treatment of multiple sclerosis wherein said antigen is a copolymer recognized by T-cells involved in the pathogenesis of multiple sclerosis.
163. (Original) The method according to claim 162 wherein said antigen is glatiramer acetate.
164. (Currently Amended) The method according to claim 135 or 136 wherein said therapeutic preparation comprises said adjuvant and an antigen useful for treatment of an autoimmune disease, a neurodegenerative disease such as Alzheimer's disease or Parkinson disease, a cancer such as melanoma, or an infectious disease such as a bacterial or viral infection.
165. (Original) A compound of the general formula:



wherein

(i) R1 is C₂₀-C₂₄ alkyl or C₁₀-C₂₄ alkenyl and A is a residue of the formula:



wherein R2 is H, C₁-C₆ alkyl, aryl, or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR₆R₇, or CR₈R₈NR₆R₇; R3 is H, a pair of electrons, or C₁-C₆ alkyl; R4 and R5 each independently is H or C₁-C₆ alkyl, or R4 and R5 together with the nitrogen atom to which they are

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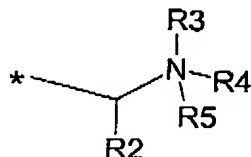
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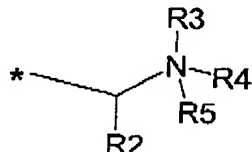
attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl; and R₆, R₇ and R₈ each independently is H or C₁-C₆ alkyl; or

(ii) R₁ is C₁₋₈ alkyl and A is a residue of the formula:



wherein R₂ is H; R₃ is a pair of electrons; and R₄ and R₅ together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl; or

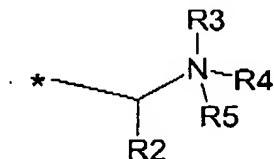
(iii) R₁ is C₁₂-C₁₆ alkyl and A is a residue of the formula:



wherein R₂ is unsubstituted aryl, or aryl or aralkyl wherein the aryl moiety is substituted by nitro, cyano, halo, hydroxy, NR₆R₇, or CR₈R₈NR₆R₇; R₃ is H, a pair of electrons, or C₁-C₆ alkyl; R₄ and R₅ each independently is H or C₁-C₆ alkyl, or R₄ and R₅ together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl; and R₆, R₇ and R₈ each independently is H or C₁-C₆ alkyl; or

(iv) R₁ is C₁₀ alkyl and A is a residue of the formula:

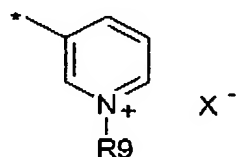
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wherein R2 is C₁-C₆ alkyl; R3 is H, a pair of electrons, or C₁-C₆ alkyl; R4 and R5 each independently is H or C₁-C₆ alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl; and R6, R7 and R8 each independently is H or C₁-C₆ alkyl; or

(v) R1 is C₁₀-C₂₄ alkyl or C₁₀-C₂₄ alkenyl and A is phenyl substituted by NR6R7 or CR8R8NR6R7, wherein R6, R7 and R8 each independently is H or C₁-C₆ alkyl, but excluding the compounds wherein R1 is C₁₀-C₁₆ alkyl and A is phenyl substituted by -CH₂-NH₂; or

(vi) R1 is C₁₀-C₂₄ alkyl or C₁₀-C₂₄ alkenyl and A is a group of the formula:



wherein R9 is C₁-C₆ alkyl or indolyl(C₁-C₆)alkyl and X⁻ is a counter ion;
 and pharmaceutically acceptable salts thereof.

166. (Original) A compound according to claim 165(i), (v) or (vi) wherein R1 is a C₁₂-C₁₈ alkenyl.

167. (Original) A compound according to claim 166 wherein R1 is a C₁₆-C₁₈ alkenyl.

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168. (Original) A compound according to claim 167 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.
169. (Original) A compound according to claim 168 wherein R2 is H or phenyl, R3 is H or a pair of electrons, and R4 and R5 are methyl or together with the N atom to which they are attached form a morpholino or a piperazine ring optionally substituted at the nitrogen atom at position 4 by methyl.
170. (Original) A compound according to claim 169 selected from the group consisting of:
- N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;
 - (4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;
 - 4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;
 - Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.
171. (Original) A compound according to claim 165(ii) wherein R1 is octadecyl and R4 and R5 together with the N atom to which they are attached form a morpholino or a piperazine ring optionally substituted at the nitrogen atom at position 4 by methyl.
172. (Original) A compound according to claim 171 which is (4-methyl-piperazin-1-yl)-acetic acid octadecyl ester tartrate.

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173. (Original) A compound according to claim 165(vi) wherein R1 is C₁₂-C₂₀ alkyl or C₁₂-C₂₀ alkenyl and A is phenyl substituted by CR₈R₈NR₆R₇, wherein R₈ is H and R₆ and R₇ is each H or C₁-C₆ alkyl.
174. (Original) A compound according to claim 173 wherein R1 is C₁₆-C₁₈ alkenyl.
175. (Original) A compound according to claim 174 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.
176. (Original) A compound according to claim 175 which is 4-dimethylaminomethyl-benzoic acid octadec-(Z)-9-enyl ester HCl or 4-dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.
177. (Original) A compound according to claim 165(vi) wherein R1 is C₁₂-C₂₀ alkyl or C₁₂-C₂₀ alkenyl.
178. (Original) A compound according to claim 177 wherein R1 is C₁₆-C₁₈ alkyl or alkenyl.
179. (Original) A compound according to claim 178 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.
180. (Original) A compound according to claim 179 selected from the group consisting of:
1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;
1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium chloride;
1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium tosylate; and

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1-[(2-(1H-indol-3-yl)-ethyl)-3-octadec-(2)-9-
enyloxycarbonyl-pyridinium bromide.

181. (Original) A compound according to claim 165(i) wherein R1 is cis-9-octadecenyl, R2 is phenyl, R3 is a pair of electrons and R4 and R is each H.

182. (Original) The compound of claim 181 which is α -amino- α -phenyl-acetic acid octadec-(2)-9-enyl ester HCl salt.

183. (Currently Amended) A pharmaceutical composition comprising a compound according to ~~any one of claims 165 to 182~~ or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

184. (Original) A pharmaceutical composition according to claim 183 for the treatment of inflammation.

185. (Currently Amended) A therapeutic composition comprising an antigen and an adjuvant according to ~~any one of claims 165 to 182~~.

186. (New) The method according to claim 136 wherein R1 is a C₁₂-C₂₀ alkyl or alkenyl.

187. (New) The method according to claim 186 wherein R1 is a C₁₆-C₁₈ alkyl or alkenyl.

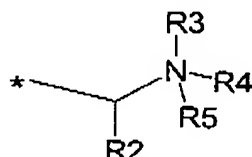
188. (New) The method according to claim 187 wherein R1 is hexadecyl, octadecyl, hexadecenyl, octadecenyl, cis-9-octadecenyl, trans-9-octadecenyl, cis-9,12-octadecadienyl, cis-6,9,12-octadecatrienyl, or cis-9,12,15-octadecatrienyl,

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189. (New) The method according to claim 183 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.

190. (New) The method according to claim 136 wherein in said compound of formula Ia the residue A is selected from the group consisting of:

(i)

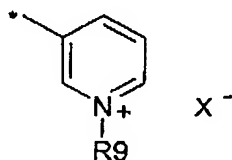


wherein R2 is H, C₁-C₆ alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR₆R₇, or CR₈R₈NR₆R₇; R3 is H, a pair of electrons or C₁-C₆ alkyl; R4 and R5 is each independently H or C₁-C₆ alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl, provided that R4 and R5 are not H or C₁-C₆ alkyl when R1 is octadecyl; and R6, R7 and R8 is each independently H or C₁-C₆ alkyl;

(ii) phenyl substituted by NR₆R₇ or CR₈R₈NR₆R₇, wherein R6, R7 and R8 each is independently H or C₁-C₆ alkyl; and

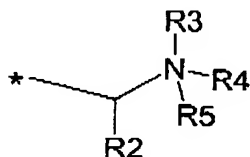
(iii)

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wherein R9 is H, C₁-C₆ alkyl or indolyl(C₁-C₄)alkyl, and X⁻ is a counter ion, or R9 is a pair of electrons and X is absent.

191. (New) The method according to claim 190 wherein the residue A has the formula:



wherein R2 is H; a straight or branched C₁-C₆ alkyl selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, pentyl and hexyl; phenyl, benzyl or p-hydroxybenzyl; R3 is H, a pair of electrons or C₁-C₆ alkyl; R4 and R5 is each independently H or C₁-C₆ alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl, said ring being selected from the group consisting of pyrrolidine, piperidine, morpholine, piperazine, and 4-methylpiperazine, provided that R4 and R5 are not H or C₁-C₆ alkyl when R1 is octadecyl.

192. (New) The method according to claim 191 wherein R2 is H or phenyl, R3 is H or a pair of electrons, R4 and R5 is

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each H or C₁-C₆ alkyl, or R₄ and R₅ together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 1 or 4 by methyl, provided that R₄ and R₅ are not H or C₁-C₆ alkyl when R₁ is octadecyl.

193. (New) The method according to claim 192 wherein said adjuvant is selected from the group consisting of:

N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;

(4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;

4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;

α -Amino- α -phenyl-acetic acid octadec-(Z)-9-enyl ester HCl salt; and

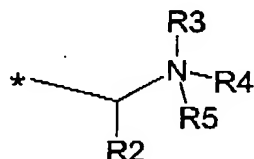
Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.

194. (New) The method according to claim 136 wherein R₁ is C₁₈ alkyl and A is a residue containing at least one cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, but excluding the compound wherein -CO-A is the residue of proline.

195. (New) The method according to claim 194 wherein the residue A has the formula:

(i)

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wherein R2 is H, C₁-C₆ alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR₆R₇, or CR₈R₈NR₆R₇; R3 is H, a pair of electrons or C₁-C₆ alkyl; R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C₁-C₆ alkyl; and R6, R7 and R8 is each independently H or C₁-C₆ alkyl.

196. (New) The method according to claim 195 wherein R2 is H or phenyl, R3 is H or a pair of electrons, and R4 and R5 together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 4 by methyl.
197. (New) The method according to claim 196 wherein said adjuvant is (4-methyl-piperazin-1-yl)-acetic acid octadecyl ester tartrate.
198. (New) The method according to claim 197 wherein A is phenyl substituted by NR₆R₇ or CR₈R₈NR₆R₇, wherein R6, R7 and R8 is each independently H or 1 C₁-C₆ alkyl.
199. (New) The method according to claim 198 wherein A is phenyl substituted by CR₈R₈NR₆R₇, wherein R8 is H and R6 and R7 is each methyl.

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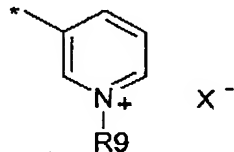
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200. (New) The method according to claim 199 wherein said adjuvant is 4-dimethylaminomethyl-benzoic acid octadec-(Z)-9-enyl ester HCl or 4-dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.

201. (New) The method according to claim 190 wherein A is the group:



wherein R9 is H, C₁-C₆ alkyl or indolyl(C₁-C₄)alkyl and X⁻ is a counter ion, or R9 is a pair of electrons and X⁻ is absent.

202. (New) The method according to claim 201 wherein R9 is a pair of electrons and X⁻ is absent, or R9 is methyl or indolyethyl and X⁻ is a counter ion selected from the group consisting of chloride, bromide, iodide and tosylate.

203. (New) The method according to claim 202 wherein said adjuvant is selected from the group consisting of:

Nicotinic acid octadec-(Z)-9-enyl ester:

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium chloride;

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium tosylate; and

1-[(2-(1H-indol-3-yl)-ethyl)-3-octadec-(Z)-9-

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enyloxycarbonyl-pyridinium bromide.

204. (New) The method according to claim 136 wherein said antigen raises a humoral response in said individual.
205. (New) The method according to claim 136 wherein said antigen raises a cellular response in said individual.
206. (New) The method according to claim 136 wherein said T-cell mediated disease is an autoimmune disease and said antigen is a peptide.
207. (New) The method according to claim 206, wherein said autoimmune disease is an organ-specific autoimmune disease.
208. (New) The method according to claim 207 wherein said organ-specific autoimmune disease is type I diabetes mellitus, multiple sclerosis, rheumatoid arthritis or autoimmune thyroiditis.
209. (New) The method according to claim 208 for the treatment of multiple sclerosis wherein said antigen is a peptide derived from the sequence of myelin basic protein (MBP) or an analogue thereof that is recognized by T-cells involved in the pathogenesis of multiple sclerosis.
210. (New) The method according to claim 209 for the treatment of multiple sclerosis wherein said antigen is a copolymer recognized by T-cells involved in the pathogenesis of multiple sclerosis.

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211. (New) The method according to claim 210 wherein said antigen is glatiramer acetate.
212. (New) The method according to claim 136 wherein said therapeutic preparation comprises said adjuvant and an antigen useful for treatment of an autoimmune disease, a neurodegenerative disease such as Alzheimer's disease or Parkinson disease, a cancer such as melanoma, or an infectious disease such as a bacterial or viral infection.